

SEP 27 2007

U.S.S.N. 10/681,627

Attorney Docket No. WYS-014.02

AMENDMENT TO THE CLAIMS

This listing of the claims will replace all prior versions, and listings, of the claims in the application.

1. (Currently amended) A method for inhibiting T cell activation ~~a response by a T cell expressing a cell surface receptor which binds a costimulatory molecule, comprising providing a T cell for which inhibition of T cell activation is desired, and contacting the T cell which has been stimulated through the TCR/CD3 complex and CD28 with an agent which inhibits production of D-3 phosphoinositides~~ phosphatidylinositol 3-kinase in the T cell, wherein contacting the T cell with the agent inhibits production of IL-2 by the T cell.
2. (Canceled)
3. (Currently amended) The method of claim 21, wherein the inhibitor of phosphatidylinositol 3-kinase is selected from a group consisting of wortmannin, quercetin and LY294002, and derivatives or analogues thereof.
4. (Canceled)
5. (Canceled)
6. (Canceled)
7. (Original) The method of claim 1, further comprising contacting the T cell with a second agent which inhibits protein tyrosine phosphorylation in the T cell.
8. (Original) The method of claim 7, wherein the second agent is an inhibitor of a protein tyrosine kinase.

U.S.S.N. 10/681,627

Attorney Docket No. WYS-014.02

9. (Original) The method of claim 8, wherein the inhibitor of a protein tyrosine kinase is herbimycin A or a derivative or analogue thereof.
10. (Withdrawn) The method of claim 7, wherein the second agent is a tyrosine phosphatase or an activator of a tyrosine phosphatase.
11. (Withdrawn) The method of claim 10, wherein the tyrosine phosphatase is a cellular tyrosine phosphatase.
12. (Withdrawn) The method of claim 11, wherein the cellular tyrosine phosphatase is CD45 or Hcph.
13. (Withdrawn) The method of claim 12, wherein the second agent is a molecule which binds to and activates CD45.
14. (Withdrawn) The method of claim 13, wherein the second agent is an anti-CD45 antibody, or fragment thereof.
15. (Currently amended) A method for inducing unresponsiveness to an antigen in a T cell ~~expressing a cell surface receptor which binds a costimulatory molecule, comprising providing a T cell for which unresponsiveness to an antigen is desired, and contacting the T cell which has been stimulated through the TCR/CD3 complex and CD28 with the antigen and an agent which inhibits production of D-3 phosphoinositides phosphatidylinositol 3-kinase in the T cell, wherein contacting the T cell with the antigen and the agent inhibits production of IL-2 by the T cell.~~
16. (Canceled)
17. (Currently amended) The method of claim ~~16~~15, wherein the inhibitor of phosphatidylinositol 3-kinase is selected from a group consisting of wortmannin, quercetin and LY294002, and derivatives or analogues thereof.

U.S.S.N. 10/681,627

Attorney Docket No. WYS-014.02

18. (Withdrawn) The method of claim 15, wherein the antigen is an alloantigen.
19. (Original) The method of claim 15, wherein the antigen is an autoantigen.
20. (Original) The method of claim 15, wherein the T cell is contacted with the antigen and the agent *in vitro* and the method further comprises administering the T cell to a subject.
21. (Withdrawn) A method of claim 20, wherein the antigen is on a surface of an allogeneic or xenogeneic cell and the subject is a recipient of an allogeneic or xenogeneic cell.
22. (Original) A method of claim 20, wherein the subject is suffering from an autoimmune disease or a disorder associated with an inappropriate or abnormal immune response.
23. (Withdrawn) A method for stimulating a response by a T cell which has received a primary activation signal and expresses a surface receptor that binds a costimulatory molecule, comprising contacting the T cell with an agent which stimulates production of D-3 phosphoinositides in the T cell.
24. (Withdrawn) The method of claim 23, wherein the agent is an activator of phosphatidylinositol 3-kinase.
25. (Withdrawn) The method of claim 23, wherein the response by the T cell comprises production of at least one lymphokine.
26. (Withdrawn) The method of claim 25, wherein the lymphokine is interleukin-2.
27. (Withdrawn) The method of claim 23, wherein the response by the T cell comprises proliferation.

U.S.S.N. 10/681,627

Attorney Docket No. WYS-014.02

28. (Withdrawn) The method of claim 23, further comprising contacting the T cell with a second agent which stimulates protein tyrosine phosphorylation in the T cell.
29. (Withdrawn) The method of claim 28, wherein the second agent is an activator of a protein tyrosine kinase.
30. (Withdrawn) The method of claim 28, wherein the second agent is an inhibitor of a cellular tyrosine phosphatase.
31. (Withdrawn) The method of claim 30, wherein the cellular tyrosine phosphatase is CD45.
32. (Withdrawn) A method for stimulating a response to an antigen by a T cell expressing a cell surface receptor which binds a costimulatory molecule comprising contacting the T cell with the antigen and an agent which stimulates production of D-3 phosphoinositides in the T cell.
33. (Withdrawn) The method of claim 32, wherein the agent is an activator of phosphatidylinositol 3-kinase.
34. (Withdrawn) The method of claim 32, wherein the antigen is a tumor-associated antigen.
35. (Withdrawn) The method of claim 32, wherein the antigen is from a pathogen selected from the group consisting of a bacteria, a virus, a fungus and a parasite.
36. (Withdrawn) The method of claim 32, wherein the T cell is contacted with the antigen and the agent *in vitro* and the method further comprises administering the T cell to a subject.
37. (Withdrawn) A method of claim 36, wherein the antigen is expressed by a tumor cell present in the subject.

U.S.S.N. 10/681,627

Attorney Docket No. WYS-014.02

38. (Withdrawn) A method of claim 36, wherein the antigen is expressed by a pathogen present in the subject.

39. (Withdrawn) A method for identifying an inhibitor of a phosphatidylinositol 3-kinase comprising:

- a) providing a T cell which expresses a receptor that binds a costimulatory molecule;
- b) stimulating an intracellular signal transduction pathway in the T cell associated with ligation of the receptor in the presence of an agent to be tested; and
- c) determining an amount of at least one D-3 phosphoinositide produced in the T cell, wherein a reduced amount of at least one D-3 phosphoinositide produced in the T cell in the presence of the agent relative to an amount produced in the T cell in the absence of the agent indicates that the agent is an inhibitor of a phosphatidylinositol 3-kinase.

40. (Withdrawn) The method of claim 39, wherein the receptor is CD28.

41. (Withdrawn) The method of claim 40, wherein the T cell is contacted with a ligand for CD28.

42. (Withdrawn) The method of claim 40, wherein the ligand for CD28 is a membrane-bound form of a B lymphocyte activation antigen selected from the group consisting of B7-1 and B7-2.

43. (Withdrawn) The method of claim 39, wherein production of at least one D-3 phosphoinositide in the T cell is measured by high pressure liquid chromatography.

44. (Withdrawn) A method for identifying an activator of phosphatidylinositol 3-kinase comprising:

U.S.S.N. 10/681,627

Attorney Docket No. WYS-014.02

- a) contacting a T cell which expresses a receptor that binds a co-stimulatory molecule with an agent to be tested; and
- b) determining an amount of at least one D-3 phosphoinositide produced in the T cell,

wherein an increased amount of at least one D-3 phosphoinositide produced in the T cell in the presence of the agent relative to an amount produced in the T cell in the absence of the agent indicates that the agent is an activator of a phosphatidylinositol 3-kinase.

45. (Withdrawn) The method of claim 44, wherein production of at least one D-3 phosphoinositide in the T cell is measured by high pressure liquid chromatography.

46. (New) The method of claim 1, wherein the inhibitor of phosphatidylinositol 3-kinase is selected from a group consisting of quercetin and LY294002, and derivatives or analogues thereof.

47. (New) The method of claim 15, wherein the inhibitor of phosphatidylinositol 3-kinase is selected from a group consisting of quercetin and LY294002, and derivatives or analogues thereof.